REMARKS

Claims 1, 6, 8 and 16 are amended to replace the phrase "in the form of" with "which is".

No new matter is presented.

I. Response to Claim Rejections - Under 35 U.S.C. § 102

A. Barry et al.

Claims 1, 3-5, 8, and 10-12 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Barry et al., PCT/GB88/00779.

Applicants traverse the rejection for the reasons of record and additionally in view of the following.

In response to the previous argument that Barry et al dose not disclose a specific embodiment in the form of a tablet or capsule, which are coated, or a core in the form of a capsule or tablet, the Examiner takes the position that the term "in the form of" can be interpreted as meaning that the gastric retention system is in the shape of a tablet or capsule.

Without conceding the merits of the rejection, the claims are amended to mention the system 'which is a tablet' or 'which is a capsule' in the independent claims. Barry et al does not disclose "a core which is a tablet" or "a core which is a capsule" as required by the currently amended independent claims. In Barry et al, the core is in the form of pellets or granules. The pellets or granules are coated with the polymers and the coated cores are further either compressed into a tablet or filled into capsules. See page, 4, lines 13-27, which teaches:

> According to the present invention there is provided a sustained-release nifedipine formulation comprising **sufficient granules** to provide a predetermined dose or number of doses of nifedipine, each of said granules having a diameter of between 0.5 and 2.5 mm and comprising: a) a core comprising 100 parts of nifedipine and from 50 to 800 parts of hydroxypropylmethyl cellulose; and b) a coating covering substantially the whole surface of the core and

> comprising 100 parts of a water insoluble but water swellable acrylic polymer and from to 70 parts of a water soluble hydroxylated cellulose derivative, the weight of the coating being from 2 to 20% of the weight of the core.

For at least this reason, Barry et al does not anticipate the presently amended claims since Barry et al does not disclose all elements of the claimed invention.

Thus applicants submit that Barry et al discloses granules, which are coated and then may be in the form of a tablet or capsule, whereas the present invention is directed to a "gastric retention system" comprising either a tablet or capsule which itself is coated.

Further, Barry et al does not have a "film capable of expanding and maintaining its physical integrity in the gastric mileu". This film is formed using a film forming polymer and an expandable component wherein the expandable component is selected from a group consisting of gas generating agent, highly swellable polymer and a superdisintegrant. The film in Barry et al does not contain a gas generating agents, and/or a superdisintegrant. It also does not contain a highly swellable polymer. This is because Barry et al uses low viscosity water soluble hydroxylated cellulose derivative like hydroxyoproyl methyl cellulose in the coating as mentioned, for instance, at page 5, line 30, and page 7, lines 19-22, which indicate the soluble nature of the hydroxylated cellulose derivative. Thus this polymer grade is **not a highly swellable polymer**. A person of skill in the art will know that the low viscosity hydroxyoproyl methyl cellulose utilized in Barry is not a highly swellable polymer as claimed in the instant case. This difference in the type and nature of the polymer grade is very clear to a person skill in the art and he or she will not consider a low viscosity hydroxyoproyl methyl cellulose as disclosed in Barry to be a highly swellable polymer. The specification of the present application clearly describes suitable highly swellable polymers are "highly swellable grades". See, for

example, page 12, line 28. This description clearly directs a person skill in the art to understand the meaning of highly swellable polymer would exclude the low viscosity polymers.

In order to anticipate a claim under 35 U.S.C. § 102, a reference must disclose within the four corners of the document not only all of the elements claimed but also all of the elements arranged or combined in the same way as recited in the claim. *Net MoneyIn, Inc. v. Verisign, Inc.*, 2008 U.S. App. LEXIS 21827, 1, 27 (Fed. Cir. 2008).

For this additional reason, Barry et al does not anticipate the currently amended claims.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

B. Egidio et al

2. Claims 1, 3-5, 8, and 10-12 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Egidio et al., U.S. Patent 5,380,533.

In response to the previous argument that Egidio et al does not teach or suggest a second coating which forms a film that is capable of expanding and maintaining its physical integrity in the gastric milieu, the Examiner takes the position that Egidio et al teaches components which fall within the definitions and examples in the specification of the claimed components and therefore, Egidio et al is expected to have the same or similar properties.

Applicants traverse the rejection.

The Examiner refers to the specification as describing:

a) film forming polymers: cellulose derivatives, acrylic acid polymers and copolymers, polymers of acrylic acid crosslinked with vinyl glycols and mixtures thereof, and

b) expandable components such as: hydroxyethylcellulose, hydroxypropylcelluloses, hydroxypropylmethylcellulose, gums, acrylic acid polymers and copolymers. See page 12, lines 2-4 and the paragraph bridging pages 12-13.

Egidio teaches a tablet or capsule with a non-protective HPMC coating followed by a gastro resistant coating. Whereas, in the present invention, which is either a coated capsule or tablet, an expandable coating is formed by applying a coating composition comprising a film-forming polymer **and** one or more expandable components on the core. Therefore, the essential features of the coating are a **film forming polymer and an expandable component**.

The Examiner states that the tablet or capsule of Egidio is coated with a non-protective film, which comprises HPMC (film forming cellulose derivative) and polyethylene glycol 6000 (swellable polymer). The Examiner is therefore equating the polyethylene glycol 6000 in the coated tablet or capsule of Egidio with the expandable component as described in the specification of the present invention.

Applicants submit that the Examiner is incorrect in drawing such a similarity because one of ordinary skill in the art would have appreciated that **polyethylene glycol 6000 is not a swellable polymer** as evidenced by the Handbook of Pharmaceutical Excipients submitted herewith as Attachment 1 to further clarify the properties of polyethylene glycol which by no means is a swellable polymer, and much less of a highly swellable grade. Polyethylene glycol 6000 is commonly used as a plasticizer in pharmaceutical coating applications. The monograph of Polyethylene glycol 6000 indicates clearly that PEG does not have swelling ability.

Further, Applicants submit that the film forming polymers of the present invention are such that the coating forms a film capable of expanding and maintaining its physical integrity in the gastric milieu. The film forming polymer (HPMC) disclosed in Egidio is described to be non

protective in nature. A person skilled in the art knows the difference between a film-forming polymer which is non protective and cannot function to provide the claimed property of a film capable of expanding and maintaining its physical integrity in the gastric milleu.

Additionally, one of the agents capable of generating internal pressure in the core, as claimed in present claim is a gas generating agent. Although, the core of Edigio includes sodium bicarbonate-a gas generating agent, since the core is coated with a coating that has only an enteric polymer but no expandable components, the sodium bicarbonate present in the core of Egidio system, will not generate any gas when the system is in the gastric retention mode, i.e., the mode in which the system is retained in the stomach . This is because the coating that contains only enteric polymer will be insoluble in the stomach contents and impermeable to gastric fluids. Edigio refers to the coating as gastroresistant throughtout its specification, for instance, column 5, lines 12-17; column 3, lines 57-60, and column 11, lines 34-36. In contrast, the coat on the gastric retention system of the present invention is not gastroresistant because it has expandable components because of which it allows ingress of the aqueous environment when the system is present in the stomach i.e., gastro retentive mode for prolonged period of time and thereby, the agent capable of generating internal pressure such as a gas generating agent can generate gas when comes in contact with aqueous gastric fluids.

Applicants would like to clarify that Comparative Example 2 of the present application, also contains "HPMC E5" and an enteric polymer. This enteric coating remains insoluble in gastric fluids. The system floats but very late (undesirable) at 7 hours. On the other hand, all the working examples 1 to 12 represent the present invention in which the coating is prepared using expandable **components such as sodium bicarbonate and sodium starch glycolate or highly swellable grade of HPMC, "HPMC K4M CR" (Table 15) and therefore floats in a short**

time in the range from about 1 min to 33 minutes. The specification of the present application clearly describes suitable highly swellable polymers that are used in the outer coating include "highly swellable grades of cellulose ethers". See, for example, page 12, line 28.

Thus, as previously pointed out, the tablets of Comparative Example 1 did not possess desirable characteristics for consistent and prolonged gastric retention as in the present invention as evidenced by the working examples, such as working Example 6 (table 15), which employs a highly swellable grade of hydroxypropyl methyl cellulose.

Thus, in view of the above and for the reasons of record which are incorporated herein by reference, the present invention is not anticipated by Egidio et al.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

C. Depui et al

Claims 1, 3-8, 10-12 and newly added claim 16 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Depui et al., U.S. Patent 6,365,184.

According to the Examiner, Depui et al. teaches formulations in the form of an enteric layer coated tablet, capsule or multiple tablet dosage form (see Abstract and Figures 1-6). The core material may be mixed with polymers including hydroxypropylmethylcellulose (i.e., highly swellable polymer), see column 9, line 13, or crosslinked polyvinylpyrrolidone, see column 12, lines 2 and 8-10. The core may be covered with a separating layer which comprises hydroxypropylmethylcellulose (highly swellable), see column 10 lines 1-15. One or more enteric layers may be further applied and include polymers such as carboxymethylethylcellulose (highly swellable) and hydroxypropylmethylcellulose phthalate (film-forming polymer) see column 10, lines 51 and 62. The core (i.e. pellets) may be further covered with an over coating layer. The

Examiner further mentions Example 15 as disclosing an embodiment with a core material comprising hydroxypropylmethylcellulose (highly swellable polymer) and a separating layer of hydroxypropylmethylcellulose (highly swellable polymer). The separating layer is further coated with an enteric coating layer which comprises a methacrylic acid copolymer (film former) and polyethylene glycol 6000 (high molecular weight polyethylene oxide swellable polymers).

Applicants traverse the rejection.

The Office Action, at page 6, states that the patent specification of the present application indicates on page 13-14 inclusion of polyethylene glycol (high molecular weight) as an expandable component. This is in error. The patent specification does not mention polyethylene glycol as the expandable component rather it lists polyethylene glycols as the plasticizers which "may be" optionally included in the expandable coating or the outer coating. Applicants sincerely request the Examiner to review pages 13-14 of the patent specification.

The Examiner further equates the enteric layer of Depui with the coating claimed (expandable coating as defined in claim 1 and claim 8 second coating as defined in claim 5, 6 and 16); of the instant invention. The Examiner states that such an enteric polymer may be further applied and includes polymers such as carboxymethylethyl cellulose (highly swellable) and hydroxypropylmethylcellulose phthalate (film-forming polymer). Applicants traverse this ground for objection, respectfully.

Depui indicates that **carboxymethylethyl cellulose** is one of the enteric polymer and NOT a highly swellable polymer. Further the enteric nature of the polymer is clearly evident from the Depui, column 10 Lines 51-63 which is recited below:

> *One or more enteric coating layers are applied onto the core material or onto the core material covered with separating layer(s) by using a*

> *suitable coating technique. The enteric coating layer material may be dispersed or dissolved in either water or in suitable organic solvents.* ***As enteric coating layer polymers*** *one or more, separately or in combination, of the following can be used, e.g. solutions or dispersions of methacrylic acid copolymers, cellulose acetate phthalate, hydroxypropyl methylcellulose phthalate, hydroxypropyl methylcellulose acetate succinate, polyvinyl acetate phthalate, cellulose acetate trimellitate, carboxymethylethylcellulose, shellac or other suitable* ***enteric coating polymer(s).***

Further, the Examiner quotes Example 15 of Depui to indicate that the enteric coating (expandable coating or second coating of the present invention) comprises a methacrylic acid copolymer (film former) and polyethylene glycol 6000 (high molecular weight polyethylene oxide swellable polymers).

Applicants submit that Example 15 of Depui, does disclose an coating which includes a enteric polymer. However, all the other ingredients (shown in the box below) do not fall within the scope of the claimed expandable components, i.e., highly swellable polymers, gas generating agents or superdisintegrants.

It is well known to a person skill in the art that the ingredients shown in the box below of Example 15 are not swellable by nature.

Example 15
Preparation of enteric coating layered pellets.

Enteric coating layer	
Pellets covered with separating layer (manufacturing and composition as in example 12)	500 g
Methacrylic acid copolymer	250 g
Polyethylene glycol 6000	75 g
Mono- and diglycerides (NF)	12.5 g
Polysorbate 80	1.2 g
Water purified	490 g

Particularly, Applicants would like to point out that polyethylene glycol 6000 is not swellable by nature as discussed above. The Examiner seems to have equated PEG polymers with polyethylene oxide polymers, in error. A person skill in the art is well aware that the two are not chemically same and in fact, exert different physical properties, their role to use in formulations is also very different. For e.g., polyethylene glycol is generally used as plasticizers, whereas polyethylene oxide is an eroding polymer and is used as a release rate controlling polymer in admixture with drugs.

Further, Depui does not teach any film-forming polymer capable of expanding and maintaining its physical integrity in the gastric milieu nor does it disclose an expandable component in the coat nor does it inherently possess any such expandable component. Therefore, the dosage form of the present invention is different from the dosage form of Depui. For at least this reason, the present invention is not anticipated by Depui.

Additionally, the Examiner states that the core of the Depui system discloses a core having hydroxypropyl methylcellulose or cross linked polyvinylpyrrolidone which falls under the meaning of agent capable of generating internal pressure in the core, as claimed in present claims. Applicants submit that although, the core of Depui includes hydroxypropyl methylcellulose or cross linked polyvinylpyrrolidone, since the core is coated with an coating that contains only an enteric polymer and NO expandable components as claimed in the present application, the hydroxypropyl methylcellulose or cross linked polyvinylpyrrolidone present in the core of Depui system, will not generate any pressure on the coat when the system is in the gastric retention mode, i.e., when located in the stomach in which the enteric polymer coating will be insoluble and impermeable to the gastric fluids. In contrast, the coating of the gastric retention system of the present invention also contains expandable components because of which it allows ingress of the aqueous environment when the system is present in the stomach for prolonged period of time and thereby, the agent capable of generating internal pressure such as a highly swellable polymer or superdisintegrant or a gas generating agent can generate internal pressure when comes in contact with aqueous fluids when the system is in the stomach.

Also Depui is not a gastric retentive system. In fact, the Depui is related to new oral pharmaceutical preparations especially for use in the treatment and prophylaxis of gastrointestinal disorders associated with the use of Non Steroidal Anti-Inflammatory Drugs (NSAIDs). For this additional reason, the present invention is not anticipated by Depui. The present invention claims a gastric retentive coated tablet or a coated capsule. The preamble of the claims clearly indicates so.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

II. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

/Jennifer M. Hayes/
Jennifer M. Hayes
Registration No. 40,641

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860

WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: June 10, 2011